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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,099	03/27/2001	Jan G.J. van de Winkel	MXI-170RCE	2545

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/820,099	VAN DE WINKEL, JAN G.J.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-12 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-12 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 January 2007 has been entered.

2. Claims 2-5 and 13-33 are cancelled.

Claim 1 has been amended.

Claim 34 has been added.

3. Claims 1, 6-12 and 34 are pending and under consideration.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Response to Arguments

6. The rejection of claims 1, 6-12 and now applied to newly added claim 34 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter is maintained. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed 1/3/2007 states that the present invention is based on the discovery that monomeric (serum) IgA binds to FcαR-expressing cells and causes elimination of (i.e., phagocytosis) of antigens bound to monomeric IgA and applicant acknowledges that the use of monomeric IgA within the claimed complexes is not only clearly and explicitly contemplated within the four corners of the present specification, but also is the central aspect of the invention. Applicant points to various parts of the as filed specification for support of monomeric IgA of the presently claimed complex.

Applicants' arguments have been fully considered but are not found persuasive. The examiner agrees that applicant's invention is based on the discovery (which may or may not be novel and non-obvious) is based upon the finding that monomeric IgA-antigen complexes are efficiently phagocytosed by FcαR-expressing cells (i.e., Kuffer cells), whereas secretory (dimeric) IgA does not initiate phagocytosis. As noted by the examiner in the previous Office Action (Advisory action mailed 12/11/2006), the specification as filed appears to provide adequate written description for (a) the administration of serum IgA (monomeric), *but not linked by chemical conjugation or recombinant genetic fusion*, with an agent or antibody that binds a target cell or antigen and causes the elimination of said target cell or antigen and (b) bispecific antibodies that bind "outside the natural ligand binding domain of the trigger receptor" (specification at pg. 9, lines 19-20) to circumvent interference by serum antibodies, wherein the linkage of the two binding components (i.e., Fab) of the bispecific antibody *are linked by chemical conjugation or recombinant genetic fusion.* The specification at pg. 3, lines 1-6, as pointed to by applicant, disclose a first portion of the complex "comprises" monomeric IgA, however, the paragraph preceding pg. 2 of the specification discloses that the molecular complex comprises "a first portion which specifically binds FcαRI expressed on liver Kupffer cells, or which specifically binds monomeric IgA or the Fc region thereof (which, in turn, binds FcαRI), linked to a second portion which specifically binds the target cell or antigen." and "In certain embodiments, the first portion of the complex binds a site on the FcαR that is distinct from the binding site for IgA, so that binding of the complex is not blocked by endogenous IgA. The first and second portions of the complex can be linked, e.g., by chemical conjugation or by genetic (recombinant) fusion." Further, at pg. 3, lines 28-32, pg. 3, line 37-pg. 4, line 2 and pg. 14, lines 30-33 as pointed to by applicant make clear that the molecular complex of the present invention comprises a first portion that specifically binds FcαRI, or monomeric IgA which binds the FcαRI, linked to a second portion which specifically binds the target cell or antigen. Thus, while it is clear that the molecular complex "comprises" monomeric IgA, the written description in the present application does not

clearly set forth that the first portion is monomeric IgA linked via chemical conjugation or by recombinant genetic fusion to a second portion that binds the target antigen. The specification as pointed to by applicant describes a "first portion", which specifically binds FcαRI or which specifically binds monomeric IgA or the Fc region thereof (see pg. 8, lines 25-29 as well as the pages pointed to by applicant). As noted by applicant the invention is based on the "discovery" that monomeric IgA-antigen complexes are phagocytosed by FcαR-expressing cells whereas dimeric IgA do not initiate phagocytosis (e.g., specification pg. 6, lines 11-17). As presently claimed, the claims recite administering a molecular complex comprising monomeric IgA linked via chemical conjugation or by recombinant genetic fusion to an agent that binds the target antigen, wherein the agent is disclosed to be a "second portion", particularly an antibody or fragment thereof (e.g., see pg. 3 of spec. and claim 6), which encompasses dimeric and polymeric IgA complexes, disclosed as not initiating phagocytosis. "[O]nly serum IgA was able to initiate phagocytosis" (spec. pg. 8, line 9).

With respect to the use of an antibody that binds outside of the natural ligand binding site for IgA as an alternative embodiment of the claimed invention, Applicant states that the examiner misconstrues the statement in applicant's specification that "serum IgA (up to 4.0mg/mL) may interfere with the activity of IgA mAbs under physiological conditions" as criticizing, discrediting or otherwise discouraging the presently claimed methods, but merely reinforces that the present specification discloses alternative embodiments. The examiner acknowledges applicant arguments regarding MPEP 2163(I)(A) that a description that does not render a claimed invention obvious cannot sufficiently describe the invention for purposes of the written description requirement of 35 U.S.C 112, citing *Eli Lilly*, 119 F.3d at 1567 (Fed. Cir. 1997). The examiner maintains that the instant specification which discloses that serum IgA may interfere with the activity of IgA mAbs under physiological conditions, and "tumor specific mAb of human IgA class are not available" (spec. pg. 9, line 7) and dimeric IgA do not initiate phagocytosis, does not provide adequate direction and guidance to the limitations currently claimed. For example, the disclosure that serum IgA may interfere

with the activity of IgA mAbs under physiological conditions would not have led the skilled artisan to utilize monomeric IgA, which mediates phagocytosis via Fc binding by FcαR-expressing cells and the disclosure that tumor specific mAb of human IgA class are not available and the fact that dimeric IgA do not initiate phagocytosis would not have led the skilled artisan to administer a complex comprising monomeric IgA linked to an antibody, i.e., dimeric IgA. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116. Applicant also states that in contrast to the findings in *Lilly*, the claimed invention is drawn to methods, which encompass a complex that is clearly described and exemplified in the specification. This has been fully considered but is not found persuasive. As discussed supra, the present invention is not clearly described and there is no exemplification of a complex comprising monomeric IgA linked to a second agent that binds a target cell or antigen, wherein the linkage occurs via chemical conjugation or by recombinant genetic fusion and wherein the administration of the complex eliminates a target cell or antigen from circulation in a subject. Again, the written description only reasonably conveys and exemplifies the initiation of phagocytosis of monomeric IgA-antigen complexes via FcαR-expressing cells (i.e., Kupffer cells), and the written description describes but does not exemplify the a complex comprising a bispecific antibody that binds FcαRI at a site distinct from the natural binding site and also binds a target cell or antigen as was known in the prior art. In addition, there is a complete lack of written description as to a method of making the claimed complex, particularly the linkage of monomeric IgA to an agent or antibody that binds a target cell or antigen. For example, is the second agent or antibody linked to a variable region or the variable regions, to the hinge region, to the CH2 region, the CH3 region of monomeric IgA, does the linkage interfere with the binding to FcαRI, does the

phrase "monomeric IgA" mean a whole monomeric IgA molecule or merely refer to the Fc region of monomeric IgA linked to a human Fv that binds the target cell or antigen?

At pg. 8 of the response, Applicant argues that the disclosure of monomeric IgA complexed with bacteria does indeed provide adequate written description for a complex comprising monomeric IgA that binds to FcαRI, linked to an agent, which specifically binds the target cell or antigen. Applicant states that antigens are recognized and bound by immune cells and therefore, capable of serving as the second binding specificity. This has been fully considered but is not found persuasive. The claims recite that the agent which specifically binds a target cell or antigen *is linked via chemical conjugation or recombinant genetic fusion*. Thus, the disclosure of an antigen bound by the monomeric IgA does not provide adequate written support for the currently claimed limitations, which require chemical linkage or recombinant genetic fusion rather than merely binding.

The examiner acknowledges applicant's remarks regarding the absence of working examples, however, the examiner maintains that while working examples and exemplification are not a prerequisite to satisfy the written description requirement, reduction to practice provides strong evidence of possession and hence, compliance with the written description requirement of 35 U.S.C 112. Conception does not occur unless one has a mental picture of the structure of the molecule, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it.

With respect to newly added claim 34, there is insufficient written support or antecedent basis for "non natural recombinant genetic fusion" as it pertains to linking a portion of monomeric IgA to a second agent that binds a target cell or antigen. Applicant points to pg. 13, lines 1-7 of the as filed specification and US Patents 5,992,845 (col. 2, lines 26-29, col. 15, lines 8-27) and 6,018,031 col. 14, lines 57-62), both specifically incorporated by reference into the present specification (e.g., pg. 13, lines 4-7). This has been fully considered, but is not found persuasive. Neither the as filed specification nor the material incorporated by reference provide adequate written support for the term "non-natural recombinant genetic fusion" of a portion of IgA and an

agent which specifically binds a target cell or antigen. The as filed specification and material incorporated by reference disclose bispecific antibodies that comprise an antigen-binding antibody fragment that binds FcαRI linked via chemical linkage or recombinant genetic fusion to a second antigen-binding antibody fragment that binds a target cell or antigen. Further, US Patents 5,992,845 and 6,018,031 do not provide adequate written support for the "portion of monomeric IgA that binds to FcαRI", which could be the Fc region of monomeric IgA linked to the Fv region of an antigen specific antibody, for example. Thus, US Patents 5,992,845 and 6,018,031 do not provide adequate written support for the limitations currently claimed. The instant disclosure does not define the term "non-natural recombinant genetic fusion" and does not provide adequate written support for "non natural recombinant genetic fusion" because it is not clearly disclosed what is included or excluded by the current claim terminology. It is noted that the only "portion of monomeric IgA" disclosed in the as filed specification as binding to FcαRI is the Fc region of monomeric IgA. Newly added claim 34 now recites limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in newly added claim 34, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in newly added claim 34 in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

New Grounds of Objections/Rejections

7. Claim 34 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 34 recites the method of base claim 1 wherein the complex comprises a portion of monomeric IgA that binds to FcαRI,

lined to an agent the specifically binds the target cell or antigen wherein the portion of monomeric IgA and the agent are linked by chemical conjugation or non-natural recombinant genetic fusion. Base claim 1 recites or requires monomeric IgA and not a "portion of monomeric IgA". Thus, claim 34 as dependent upon base claim 1 does not include every limitation of the claim on which it depends. Any claim which is in dependent form but which is so worded that it, in fact is not, as, for example, it does not include every limitation of the claim on which it depends, will be required to be canceled as not being a proper dependent claim. See MPEP 608.01(n)(II).

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: there is insufficient antecedent basis for the term "non-natural recombinant genetic fusion". Applicants' attention is directed to the new matter rejection in item no. 6 above.

9. Claims 1 and 6-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of eliminating a target cell or antigen from the circulatory system of a subject comprising administering monomeric (serum) IgA or administering a bispecific antibody comprising an antibody fragment that binds FcαRI outside the natural ligand binding domain and an antibody fragment that binds a target cell or antigen, wherein the antibody fragments of the bispecific antibody are linked via chemical conjugation or by recombinant genetic fusion, does not reasonably provide enablement for a method of eliminating a target cell or antigen from the circulatory system of a subject comprising administering monomeric IgA linked via chemical conjugation or recombinant genetic fusion to a second agent that binds a target cell or antigen as embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to a method of eliminating a target cell or antigen from the circulatory system of a subject comprising administering monomeric IgA linked via chemical conjugation or recombinant genetic fusion to a second agent that binds a target cell or antigen wherein the target cell is a cancer cell or the antigen is a bacterial, viral or fungal antigen. Thus, the claims encompass the administration of monomeric IgA linked to an antibody or antibody fragment that binds a target cell or antigen, which broadly reads upon dimeric IgA since dimeric IgA is merely one interpretation of monomeric IgA linked to an antibody. Further, the claims encompass the use of monomeric IgA for the treatment of cancer and the Fc-mediated phagocytosis by FcαR-expressing Kupffer cells.

The specification does not provide a sufficiently enabling description of the claimed invention. The specification teaches that the administration of serum IgA (monomeric) complexed, *but not linked by chemical conjugation or recombinant genetic fusion*, with antigen as causing the elimination of antigens bound to monomeric IgA and (b) bispecific antibodies that bind "outside the natural ligand binding domain of the trigger receptor" (specification at pg. 9, lines 19-20) to circumvent interference by serum antibodies, wherein the two binding components (i.e., Fab) of the bispecific antibody are linked by chemical conjugation or recombinant genetic fusion. The specification also discloses that tumor specific mAb of human IgA class are not available and serum IgA may interfere with the activity of IgA mAbs under physiological conditions (pg. 9). The

specification teaches that dimeric IgA (SIgA) was unable to initiate phagocytosis 9see pg. 8). The specification does not teach a method of eliminating a target cell or antigen, inclusive to a cancer cell, a bacterial, viral or fungal antigen comprising administering monomeric IgA that binds to FcαRI linked to an agent or antibody that binds said target cell or antigen. There are no working examples of a method of eliminating a target cell or antigen, inclusive to a cancer cell, a bacterial, viral or fungal antigen comprising administering monomeric IgA that binds to FcαRI linked to an agent or antibody that binds said target cell or antigen. Thus, the scope of the claims is broad relative the description and enablement of the present application. The scope of the claims must bear a reasonable correlation with the scope of enablement. See *In re Fisher*, 166 USPQ 19 24 (CCPA 1970).

The state of the prior art is such that a single class of IgA FcR binds to monomeric IgA, known as FcαRI or CD89. FcαRI binds both antigen-complexed and monomeric IgA1 and IgA2 and cross-linking of FcαRI on myeloid effector cells by polymeric IgA, IgA immune complexes, or mAbs specific for epitopes within or outside the ligand-binding domain stimulates degranulation, superoxide release, secretion of inflammatory cytokines, endocytosis and phagocytosis. (Deo et al, The Journal of immunology, 160:1677-1686, 1998, IDS reference field 1/22/2002). Deo et al and Huls et al (Cancer Research, 59:5778-5784, November 15, 1999, IDS reference filed 1/22/2002) consistent with the instant specification teach that tumor-specific mAbs of human IgA class are not available (Deo et al, pg. 1677, 2nd col. and Huls et al, pg. 5778, 2nd col.). Further, there are several conflicting reports that describe either the ability or disability of secretory IgA (SIgA) (i.e., dimeric IgA) to trigger functions like phagocytosis. Kerr M. A. Biochem. J. 271:285-296, 1990; Weisbart et al, Nature 332:647-648, 1988, IDS reference filed 8/3/2001; Nikolova et al, Journal of Leukocyte Biology, 57:875-882, 1995; Gorter et al, Immunology, 61:303-309, 1987. Thus, the state of the art recognized that it would be highly unpredictable to administer monomeric IgA linked to an antibody (i.e., dimeric IgA) that binds a target cell or antigen for eliminating the target cell or antigen from the cuirculatory system of a subject, particularly where the target

cell is a cancer cell in view that tumor-specific mAbs of human IgA class were not available. There is insufficient guidance and direction to assist those skilled in the art in practicing the claimed invention comprising administering dimeric IgA (i.e., monomeric IgA linked to an antibody), which does not initiate FcαRI-mediated phagocytosis according to the teachings provided in applicants specification. There is no guidance or direction to assist those skilled in the art in producing a monomeric IgA linked to an antibody or antibody fragment thereof for eliminating a target cell or antigen from the cuirculatory system of a subject. One of skill in the art would not know whether the linkage of the antibody or antibody fragment thereof that binds a target cell or antigen to monomeric IgA affects binding to FcαR and subsequently FcαRI-mediated phagocytosis. One of skill in the art would neither expect nor predict the appropriate functioning of the claimed complexes comprising monomeric IgA linked to an antibody or antibody fragment thereof as broadly as is claimed.

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Deo et al, Huls et al, Kerr M. A., Weisbart et al, Nikolova et al and Gorter et al the lack of guidance and direction provided by applicant, and lack of working examples of monomeric IgA linked to an antibody (i.e., dimeric IgA) that binds a target cell or antigen for eliminating the target cell or antigen from the cuirculatory system of a subject, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods, commensurate in scope with the claimed invention.

10. The rejection of claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by van Spriel et al (Journal of Infectious Diseases, 179(3):661-669, 1999, first publicly available date of 3/3/1999).

It is noted that this rejection is already of record, was withdrawn in view of amendments to the claims, and is not being reapplied in view of newly added claim 34. Further, it is noted that the van Spriel et al reference was cited in the office Action

mailed 1/26/2006, however, it appears that the reference was never cited on the PTO-892. Accordingly, the reference is being cited on the PTO-892 accompanying this Office Action.

The claims are interpreted as being drawn to a method for eliminating a target cell or antigen from the circulatory system of a subject comprising administering to the subject a complex comprising a portion of monomeric IgA that binds to FcαRI, linked to an agent that binds a target cell or antigen wherein the portion of monomeric IgA and the agent are linked by chemical conjugation or non-natural recombinant genetic fusion.

van Spriel et al teach a method of treating a fungal infection in a subject comprising administering G-CSF followed by injection of a bispecific antibody comprising a FcαRI F(ab) fragment chemically linked to *C. albicans* directed $F(ab')_2$ fragments, which effectively enhanced the killing (i.e., elimination) of *C. albicans* (see entire document, particularly pages 664-665). Thus, A portion of monomeric IgA that binds to FcαRI broadly embraces Fab fragments that bind to FcαRI, since a Fab fragment is a "portion" of monomeric IgA. Applicant is reminded that the isotypic determinants or heavy chain antigenic determinants unique to IgA are found in the constant regions, not the antigen-binding portion and as such, the Fab of the prior art necessarily possesses the characteristics of the antigen-binding antibody fragment (i.e., portion) of monomeric IgA. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Thus, van Spriel et al anticipates the claim.

11. Claim 34 is rejected under 35 U.S.C. 102(e) as being anticipated by Deo et al (US Patent 5,922,845, filed 7/11/1996, cited on PTO-892 mailed 1/26/2006.

The claim has been described supra.

It is noted that this rejection is already of record, was withdrawn in view of amendments to the claims, and is not being reapplied in view of newly added claim 34.

Doe et al teach a method of eliminating an unwanted cell in a subject comprising administering a mutlispecific molecule comprising an FcαRI specific antigen-binding fragment (i.e., Fab, Fab', $F(ab')_2$, Fv or single-chain Fv) linked via chemical conjugation

or recombinant genetic fusion (i.e., "non-natural") to an antibody or antigen-binding fragment thereof that binds a bacteria, virus, fungi or cancer cell (see entire document, particularly col. 2, lines 26-32, col. 4, lines 10-26, col. 10, col. 11, lines 18-36, col. 12-14, col. 21, lines 35-43 and Examples). Applicant is reminded that the isotypic determinants or heavy chain antigenic determinants unique to IgA are found in the constant regions, not the antigen-binding portion and as such, the antigen-binding antibody fragments of the prior art necessarily possess the characteristics of the antigen-binding antibody fragment (i.e., portion) of monomeric IgA. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Thus, Doe et al anticipates the claim.

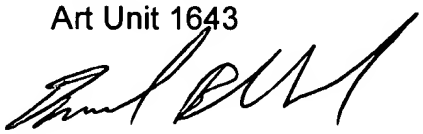
12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard
Patent Examiner
Art Unit 1643



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March 13, 2007